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FILE COVERS 1947 - 18 Oct 2001 VOL 135 ISS 17  
FILE LAST UPDATED: 17 Oct 2001 (20011017/ED)

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L1	468	SEA FILE=REGISTRY PROSTATE CANCER ANTIGEN?
L2	1534	SEA FILE=REGISTRY (MRNA/BI OR MRNABP/BI OR MRNASE/BI)
L3	66	SEA FILE=REGISTRY MONOCLONAL ANTIBOD?/CN
L4	6698	SEA FILE=HCAPLUS L1 OR (PROSTAT?(W)CANCER?(W)ANTIGEN? OR PCA)
L5	196398	SEA FILE=HCAPLUS L2 OR MRNA
L6	384631	SEA FILE=HCAPLUS L3 OR MONOCLONAL(W)ANTIBOD? OR AB# OR MAB#
L9	60	SEA FILE=HCAPLUS L4(W) (3 OR III)
L11	70	SEA FILE=HCAPLUS L9 OR PCA3 OR PCAIII
L12	2	SEA FILE=HCAPLUS L6 AND L11
L13	418295	SEA FILE=HCAPLUS L5 OR (RNA OR RIBONUCLEIC(W)ACID?)
L14	2	SEA FILE=HCAPLUS L13 AND L11
L15	3	SEA FILE=HCAPLUS L12 OR L14
L17	9	SEA FILE=HCAPLUS L11 AND (?HYBRID? OR QUANTIF? OR PROMOT? OR CONJUG? OR DIAGN?)
L18	10	SEA FILE=HCAPLUS L17 OR L15

=> d ibib abs hitrn l18 1-10

L18 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 2001:247483 HCAPLUS  
DOCUMENT NUMBER: 134:279102  
TITLE: **PCA3 mRNA** species in benign and malignant prostate tissues and methods for specifically **diagnosing** prostate cancer

M. Smith 308-3278

INVENTOR(S): Busse, Ursula; Chypre, Camille; Fradet, Yves  
PATENT ASSIGNEE(S): Diagnocure Inc., Can.  
SOURCE: PCT Int. Appl., 60 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023550	A2	20010405	WO 2000-CA1154	20000929
WO 2001023550	A3	20010816		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 1999-156594 P 19990929

AB This invention concerns the discovery of two distinct **PCA3** mRNA sequences. One of these sequences corresponds to a short **PCA3 mRNA** mol. whereas the other **PCA3 RNA** mol. is longer as it comprises an addnl. sequence between exon 3 and exon 4a. The short **RNA** is assocd. with prostate cancer whereas the long **RNA** sequence is assocd. with a non-malignant state of the prostate. Based on the differential expression levels of these two **PCA3 RNA** sequences, protocols for the **diagnosis** of prostate disease are provided. The invention also relates to therapeutic approaches to prostate cancer.

L18 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:861924 HCAPLUS  
DOCUMENT NUMBER: 134:40682  
TITLE: Breast, gastric and prostate cancer-associated antigens and their diagnostic and therapeutic uses  
INVENTOR(S): Obata, Yuichi  
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA  
SOURCE: PCT Int. Appl., 799 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073801	A2	20001207	WO 2000-US14749	20000526
W:	AU, CA, CN, JP, KR, US			
RW:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			

PRIORITY APPLN. INFO.:

US 1999-136526 P 19990528  
US 1999-153454 P 19990910

AB Cancer-assocd. antigens have been identified by autologous antibody screening of libraries of nucleic acids expressed in breast, gastric, and prostate cancer cells using antisera from cancer patients. The invention relates to 593 nucleic acids and 740 encoded polypeptides which are cancer-assocd. antigens expressed in patients afflicted with cancer. The invention provides, inter alia, isolated nucleic acid mols., expression vectors contg. those mols., and host cells transfected with those mols. The invention also provides isolated proteins and peptides, antibodies to those proteins and peptides and cytotoxic T lymphocytes which recognize the proteins and peptides. Fragments of the foregoing including functional fragments and variants also are provided. Kits contg. the foregoing mols. addnl. are provided. The mols. provided by the invention can be used in the diagnosis, monitoring, research, or treatment of conditions characterized by the expression of one or more cancer assocd. antigens.

L18 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:433333 HCAPLUS  
DOCUMENT NUMBER: 131:238480  
TITLE: Construction and identification of replication-deficient human thrombopoietin recombinant adenoviruses  
AUTHOR(S): Liu, Lin; Luo, Chengji; Su, Yongping  
CORPORATE SOURCE: Xinqiao Hospital, Third Military Medical University, Chungking, 400037, Peop. Rep. China  
SOURCE: Di-San Junyi Daxue Xuebao (1999), 21(5), 314-317  
CODEN: DYXUE8; ISSN: 1000-5404  
PUBLISHER: Di-San Junyi Daxue  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

AB The authors constructed replication-deficient human thrombopoietin (TPO) recombinant adenoviruses (AdCMVTPO). The full-length human TPO cDNA was cloned down stream of human CMV promoter of adenoviral shuttle plasmid **pCA3**. Then the resultant **pCA3**-TPO plasmid was cotransfected into 293 cells with the plasmid pBHG10 carrying the adenoviral genome. Plasmid AdCMVTPO was successfully generated with homologous recombination. A549 cells were infected with AdCMVTPO and the expression of human TPO was evaluated in vivo. The titer of AdCMVTPO reached 4.5 .times. 10<sup>9</sup> pfu/mL after amplification in 293 cells. A549 cells expressed high level of human TPO after infection. The recombinant adenovirus maybe used in the gene therapy of hemopoietic reconstruction.

L18 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:682508 HCAPLUS  
DOCUMENT NUMBER: 129:299040  
TITLE: Prostate cancer antigen **PCA3**, **pCA3** cDNA and **diagnosis** and treatment of prostate cancer  
INVENTOR(S): Bussemakers, Marion J. G.  
PATENT ASSIGNEE(S): Diagnocure Inc., Can.  
SOURCE: PCT Int. Appl., 112 pp.  
CODEN: PIXXD2

M. Smith 308-3278

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9845420	A1	19981015	WO 1998-CA346	19980409
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9870194	A1	19981030	AU 1998-70194	19980409
EP 1007650	A1	20000614	EP 1998-916696	19980409
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			

PRIORITY APPLN. INFO.: US 1997-41836 P 19970410  
WO 1998-CA346 W 19980409

AB The present invention relates, in general, to a prostate cancer antigen, **PCA3**. In particular, the present invention relates to nucleic acid mols. coding for the **PCA3** protein; purified **PCA3** proteins and polypeptides; recombinant nucleic acid mols.; cells contg. the recombinant nucleic acid mols.; antibodies having binding affinity specifically to **PCA3** proteins and polypeptides; ~~hybridomas contg. the antibodies; nucleic acid probes for the~~ detection of nucleic acids encoding **PCA3** proteins; a method of detecting nucleic acids encoding **PCA3** proteins or polypeptides in a sample; kits contg. nucleic acid probes or antibodies; bioassays using the nucleic acid sequence, protein or antibodies of this invention to **diagnose**, assess, or prognose a mammal afflicted with prostate cancer; therapeutic uses; and methods of preventing prostate cancer in an animal. Differential display anal. was used to identify genes overexpressed in prostatic carcinomas in comparison to normal prostate. One such gene encoding **PCA3** exhibited at least 4 different transcripts due to alternative splicing. This gene was mapped to human chromosome 9q21-22. A homolog of the gene was found in monkey, cow, horse, sheep, goat, pig, dog and cat. A semi-quant. RT-PCR anal. allowed a clear distinction between benign and malignant prostate samples in 23 of 25 cases. At least a 20-fold overexpression of **PCA3** in prostatic carcinomas as compared to normal or benign prostatic hyperplasia was obsd. The level of expression of **PCA3** tended to be pos. correlated with tumor grade.

L18 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1993:250452 HCAPLUS

DOCUMENT NUMBER: 118:250452

TITLE: Simultaneous binding of nitric oxide and isotopically labeled substrates or inhibitors by reduced protocatechuate 3,4-dioxygenase

AUTHOR(S): Orville, Allen M.; Lipscomb, John D.

M. Smith 308-3278

CORPORATE SOURCE: Med. Sch., Univ. Minnesota, Minneapolis, MN, 55455,  
USA

SOURCE: J. Biol. Chem. (1993), 268(12), 8596-607  
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The active site of Fe<sup>3+</sup> of protocatechuate (PCA) 3,4-dioxygenase can be nonenzymically reduced to Fe<sup>2+</sup>, to give a colorless and EPR-silent enzyme (Er). NO binds to Er to yield a species with EPR (S = 3/2; g = 4.341, 3.693, 1.984; E/D = 0.055) and optical absorption ( $\lambda_{\text{max}}$  = 430 nm,  $\epsilon$  = 1870 M<sup>-1</sup> cm<sup>-1</sup>/iron) spectra. Addn. of NO to a preformed Er.cntdot.PCA complex results in a new species (EPR: S = 3/2; g = 4.920, 2.988, 1.846; E/D = 0.175; optical;  $\lambda_{\text{max}}$  = 404 nm,  $\epsilon$  = 3930 M<sup>-1</sup> cm<sup>-1</sup>/iron). Hyperfine broadening from the substrates [17O]PCA or [17O]homoprotocatechuate (HPCA) is obsd. in the EPR spectra of Er.cntdot.substrate.cntdot.NO complexes only when the 17O (I = 5/2) is placed in the carbon-4 OH group, suggesting that only this group binds to the iron when NO is bound. Previous studies showed that both OH groups of HPCA can bind to the Fe<sup>3+</sup> of the oxidized enzyme. Thus, the NO may compete with the substrate carbon-3 OH group for a binding site on the Fe<sup>2+</sup>. In contrast, when either PCA or HPCA is added to a preformed Er.cntdot.NO complex, no substrate binding to the Fe<sup>2+</sup> is detected. At 2.3 K, white light photodissociates NO from the Er.cntdot.NO and Er.cntdot.PCA.cntdot.NO complexes. The Er.cntdot.NO complex is photodissociated to a greater extent than the Er.cntdot.PCA.cntdot.NO complex, and different NO rebinding kinetics are obsd. showing that the substrate strongly influences the photodissocn./reassocn. process. Photodissocn. of each complex results in the formation of some Fe<sup>3+</sup>, suggesting that the nitrosyl complex has at least partial Fe<sup>3+</sup>-NO-character. In soln. at 5-10.degree., white light **promotes** conversion of preformed Er.cntdot.NO plus PCA to the Er.cntdot.PCA.cntdot.NO complex, suggesting that formation of the latter complex requires dissocn. of NO. It is proposed that initial NO binding blocks the single site for exogenous ligand binding of the iron, thereby inhibiting PCA assocn. In contrast, PCA binding before NO appears to evoke an enzyme conformational change that allows simultaneous NO binding in another ligand site. These results are consistent with the current model for the mechanism of intradiol dioxygenases in which a PCA-induced conformational change allows substrate to bind as an Fe<sup>3+</sup> chelate and O<sub>2</sub> reacts initially with the PCA rather than the Fe<sup>3+</sup>.

L18 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1993:94309 HCAPLUS

DOCUMENT NUMBER: 118:94309

TITLE: Cloning of cDNAs for calcium channel subtypes specific  
for human neuronal tissue and their use

INVENTOR(S): Franz, Juergen; Weingaertner, Bernhard; Unterbeck,  
Axel; Rae, Peter

PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Eur. Pat. Appl., 101 pp.  
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

M. Smith 308-3278

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 507170	A2	19921007	EP 1992-104970	19920323
EP 507170	A3	19921119		
EP 507170	B1	19970115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 4110785	A1	19921008	DE 1991-4110785	19910404
AT 147781	E	19970215	AT 1992-104970	19920323
ES 2097231	T3	19970401	ES 1992-104970	19920323
JP 05320194	A2	19931203	JP 1992-103753	19920331
US 6229000	B1	20010508	US 1995-456200	19950531

PRIORITY APPLN. INFO.: DE 1991-4110785 A 19910404  
 US 1992-858278 B2 19920326  
 US 1993-64778 B2 19930519  
 US 1993-94712 B1 19930719

AB cDNAs from human nervous tissue that cross-hybridize with a cDNAs for subunits of the Ca channel of carp skeletal muscle or of human are cloned and characterized. These cDNAs are useful in the testing of specific antagonists of the individual Ca channel subtypes (no data). The cDNAs were obtained by screening com. cDNA banks from human nervous tissue.

L18 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:567599 HCAPLUS

DOCUMENT NUMBER: 117:167599

TITLE: Identification of open reading frames of chicken anemia virus for use in vaccines and diagnostic reagents

INVENTOR(S): Sondermeijer, Paulus Jacobus Antonius; Claessens, Johannes Antonius Joseph

PATENT ASSIGNEE(S): AKZO N. V., Neth.

SOURCE: Eur. Pat. Appl., 25 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 483911	A2	19920506	EP 1991-202737	19911023
EP 483911	A3	19930224		
R: BE, CH, DE, ES, FR, GB, GR, IT, LI, NL, SE				
ZA 9108426	A	19921230	ZA 1991-8426	19911022
CA 2054542	AA	19920501	CA 1991-2054542	19911030
AU 9186888	A1	19920507	AU 1991-86888	19911030
CN 1062168	A	19920624	CN 1991-111520	19911030
CN 1041326	B	19981223		
JP 05086088	A2	19930406	JP 1991-286877	19911031
HU 62325	A2	19930428	HU 1991-3433	19911031
US 5554525	A	19960910	US 1992-917722	19920720

PRIORITY APPLN. INFO.: US 1990-605881 19901031

AB Open reading frames (ORFs) of chicken anemia virus are cloned for use in vaccine development (no data) and **diagnostics**. Purified replicative form of the virus was cloned in pGEM7zf+ and sequenced. ORF 1 was placed under the control of the long terminal repeat sequence of Rous sarcoma virus and introduced into herpesvirus of turkey by in vivo recombination in chick embryo fibroblasts. Cells presenting chicken anemia virus antigens were obtained.

L18 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:226879 HCAPLUS  
DOCUMENT NUMBER: 114:226879  
TITLE: Reduced calcium sensitivity of dihydropyridine binding to calcium channels in spontaneously hypertensive rats  
AUTHOR(S): Ebata, Hitoshi; Natsume, Takashi; Mitsunashi, Takeshi; Yaginuma, Toshio  
CORPORATE SOURCE: Dep. Cardiol., Jichi Med. Sch., Tochigi, 329-04, Japan  
SOURCE: Hypertension (Dallas) (1991), 17(2), 234-41  
CODEN: HPRTDN; ISSN: 0194-911X  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB To explore the role of calcium channels in hypertension, dihydropyridine ([<sup>3</sup>H]PN200-110) binding to heart, brain, and skeletal muscle microsomes of 4-, 8- and 15-wk-old spontaneously hypertensive rats (SHR) and Wistar-Kyoto (WKY) rats was measured. At a const. Ca<sup>2+</sup> ion concn. (pCa 3.0), maximal binding (B<sub>max</sub>) of dihydropyridine binding to heart and brain microsomes was enhanced in 8- and 15-wk-old SHR compared with WKY rats, whereas this phenomenon was not obsd. in 4-wk-old SHR and WKY rats. B<sub>max</sub> and dissocn. const. (K<sub>d</sub>) values for skeletal muscle microsomes from SHR showed no difference compared with WKY rats irresp. of age. Dihydropyridine binding to heart microsomes, brain microsomes, and solubilized skeletal muscle microsomes exhibited strong calcium dependence. The Ca<sup>2+</sup>-dependent dihydropyridine binding curves for heart showed a Hill slope, and pK 0.5 values for 15-wk-old SHR and WKY rats were 0.70 and 4.66 vs. 0.72 and 5.66, resp., indicating that 15-wk-old SHR require 10-fold higher calcium concn. than WKY rats to **promote** dihydropyridine binding. The pK 0.5 values of calcium for brain and solubilized skeletal muscle calcium channels in 15-wk-old SHR were also lower than in WKY rats. This difference first became apparent in SHR and WKY rats as early as 4 and 8 wk after birth. These results suggest that enhancement of calcium channel d. might occur in the heart and brain of SHR in response to elevated blood pressure and that reduced calcium sensitivity of dihydropyridine binding to calcium channels might be a primary characteristic of this rat strain.

L18 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:37989 HCAPLUS  
DOCUMENT NUMBER: 114:37989  
TITLE: Annexin-chromaffin granule membrane interactions: a comparative study of synexin, p32 and p67  
AUTHOR(S): Zaks, William J.; Creutz, Carl E.  
CORPORATE SOURCE: Mol. Biol. Inst., Univ. Virginia, Charlottesville, VA, 22908, USA  
SOURCE: Biochim. Biophys. Acta (1990), 1029(1), 149-60  
CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The chromaffin granule membrane binding and aggregating properties of 3 annexins, synexin, p32, and p67, were studied and compared. Each protein was activated to bind and aggregate membranes with a biphasic  $\text{Ca}^{2+}$  dependence, with 1 phase titrating between pCa 5.0-3.5 and the 2nd at higher levels of  $\text{Ca}^{2+}$  (pCa <3.5). Addn. of cis-unsatd. free fatty acids lowered these  $\text{Ca}^{2+}$  requirements by .apprx.1 log unit.  $\text{Ba}^{2+}$  and  $\text{Sr}^{2+}$  were able to partially substitute for  $\text{Ca}^{2+}$ , with the order of sensitivity  $\text{Ca}^{2+} > \text{Sr}^{2+} > \text{Ba}^{2+}$ . The proteins appeared to bind to distinct but overlapping populations of receptor sites, and did so in a manner displaying pos. cooperativity at the higher  $\text{Ca}^{2+}$  levels. The maximal efficacy of the proteins as membrane aggregators differed with synexin being 1-2 fold more efficacious than p32, which in turn was 7-fold more efficacious than p 67. In combination, p67 was an effective inhibitor of granule aggregation induced by synexin or p32, whereas p32 was able to both **promote** and inhibit synexin-induced granule aggregation in a manner which varied with synexin concn. The complexity of these annexin-membrane interactions may be a reflection of the multidomain structure of the annexins and may have implications for the differential functions of these proteins in cells.

L18 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1983:484852 HCAPLUS

DOCUMENT NUMBER: 99:84852

TITLE: Effect of various levels of external pCa on the barium-induced motor responses of Paramecium caudatum

AUTHOR(S): Janiszewski, Janusz

CORPORATE SOURCE: Inst. Biol., N. Copernicus Univ., Torun, 87100, Pol.

SOURCE: Acta Protozool. (1982), 21(3-4), 221-6

CODEN: ACPZAU; ISSN: 0065-1583

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The influence of the **abs.**  $\text{Ca}^{2+}$  concn. in the medium on the Ba-induced motor responses of P. caudatum was investigated. Motor reactions of paramecia were recorded by a long-exposure dark-field photomacrog. technique. A series of expts. were performed at external Ca levels of 1 mmol  $\text{CaCl}_2$  (pCa 3) and 10 mmol  $\text{CaCl}_2$  (pCa 2). When the initial ratio  $[\text{Ba}^{2+}]:[\text{Ca}^{2+}]$  was 0.25, both at pCa 3 and pCa 2, >80% of ciliates showed periodic ciliary reversal (PCR), whereas in the range of ratio 0.25-2, at pCa 3, the percentage of paramecia responding with PCR decreased and that showing continuous ciliary reversal (CCR) increased. However, at pCa 2, the percentage of ciliates showing PCR was const. in the whole range of  $[\text{Ba}^{2+}]:[\text{Ca}^{2+}]$  concn. ratios, with a slight increase in the no. of animals responding with CCR at higher ratios. The hypothesis that membrane Ca channels are inactivated by Ca deposited at the inner side of ciliary membrane is supported.



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?show files

File 5:Biosis Previews(R) 1969-2001/Oct W2

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File 20:World Reporter 1997-2001/Oct 18

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File 351:Derwent WPI 1963-2001/UD,UM &UP=200160

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File 357:Derwent Biotechnology Abs 1982-2001/Dec B1

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Set	Items	Description
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S1	8	((PROSTAT?(W)CANCER?(W)ANTIGEN OR PROSTAT?(W)CANCER?(W)AG? ? OR PCA)(W)(3 OR III) OR PCA3 OR PCAIII)(5N)(HYBRID? OR QUAN- TIF? OR PROMOT? OR CONJUG? OR DIAGN? OR DX OR MONOCLONAL OR A- B? ? OR MAB? ?)
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S2	8	RD (unique items)
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?t2/3 ab/1-8

2/AB/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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11414140 BIOSIS NO.: 199800195472

DiagnoGene PCA3 reliable NASBA based reagents for detecting PCA3 mRNA,  
a recently described prostate marker.

AUTHOR: Tamimi Y; Busse U; Menard C; St-Amand J; Chypre C; Fradet Y

AUTHOR ADDRESS: DiagnoCure, 2050 bd. Rene Levesque, Ste Foy, PQ G1V 2K8\*\*  
Canada

~~JOURNAL: Proceedings of the American Association for Cancer Research Annual  
Meeting 39p234 March, 1998~~

CONFERENCE/MEETING: 89th Annual Meeting of the American Association for  
Cancer Research New Orleans, Louisiana, USA March 28-April 1, 1998

SPONSOR: American Association for Cancer Research

ISSN: 0197-016X

RECORD TYPE: Citation

LANGUAGE: English

1998

2/AB/2 (Item 1 from file: 20)

DIALOG(R)File 20:World Reporter

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18878796

DiagnoCure launches automated ImmunoCyt(TM) project

CANADA NEWSWIRE

September 18, 2001

JOURNAL CODE: WCNW LANGUAGE: English RECORD TYPE: FULLTEXT

WORD COUNT: 643

Ticker Symbol: CUR

QUEBEC CITY, QC, Sept. 18 /CNW/ - DiagnoCure Inc. (TSE: CUR), an  
emerging biotechnology company specializing in the development of  
early-stage cancer diagnostics, today announced a collaborative program,  
involving its U.S. distribution partner, DAKO Corporation (DAKO) and  
Applied Imaging Corp. (Nasdaq NM: AICX) to automate the image analysis  
component of the Company's commercialized test for bladder cancer,  
ImmunoCyt(TM).

2/AB/3 (Item 2 from file: 20)  
DIALOG(R)File 20:World Reporter  
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10437109  
DiagnoCure Announces Annual Shareholders' Meeting and Results of First  
Quarter  
CCN DISCLOSURE  
April 05, 2000  
JOURNAL CODE: WCCN LANGUAGE: English RECORD TYPE: FULLTEXT  
WORD COUNT: 1251

QUEBEC, QUEBEC--During its annual shareholders' meeting, Serge Pitre, President of DiagnoCure, emphasized that the very large commercial potential of the uPM3(TM) test could require a licensing agreement with a large, international company that is well established in the diagnostic market. This market is estimated at approximately 30 million tests per year in the United States alone, according to the April 1998 issue of Future Oncology, in addition to a similar number in the rest of the world. The uPM3 test, the first in the DiagnoGene series of tests for the detection of nucleic acids expressed in cancers, is based on the PCA3 gene for which DiagnoCure holds all commercial rights worldwide.

Dr. Yves Fradet, Executive Vice President of the Company, explained that the uPM3 test could probably reduce significantly the number of biopsies carried out needlessly among patients with a PSA result that is low or only moderately high. He also indicated that DiagnoCure intends to create new test prototypes with the DiagnoGene(TM) kit for the diagnosis of other common cancers for which no tests currently exist. The Company also intends to develop therapeutic applications of PCA3 gene technology with the ability to block the presumed activity of the PCA3 gene in prostatic cancer cells. As for targeted nanoErythrocytes using fusion proteins, research is providing very encouraging results and, in due time, DiagnoCure will enhance the potential of this multi-faceted technological platform through licensing agreements or strategic alliances.

2/AB/4 (Item 3 from file: 20)  
DIALOG(R)File 20:World Reporter  
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09412787  
Important Breakthrough for DiagnoCure in Prostate Cancer Field  
CANADIAN CORPORATE NEWS  
February 02, 2000  
JOURNAL CODE: WCCN LANGUAGE: English RECORD TYPE: FULLTEXT  
WORD COUNT: 740

MONTREAL, QUEBEC--  
Preliminary Data Confirm Potential of New Prostate Cancer Marker  
Developed by DiagnoCure

2/AB/5 (Item 1 from file: 351)  
DIALOG(R)File 351:Derwent WPI  
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013773921  
WPI Acc No: 2001-258132/200126  
XRAM Acc No: C01-077853

XRPX Acc No: N01-184090

Novel nucleic acid encoding differentially expressed prostate cancer antigen 3 mRNA containing additional sequence giving rise to long PCA3 mRNA, useful for diagnosis of mammal afflicted with prostate cancer

Patent Assignee: DIAGNOCURE INC (DIAG-N)

Inventor: BUSSE U; CHYPRE C; FRADET Y

Number of Countries: 094 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200123550	A2	20010405	WO 2000CA1154	A	20000929	200126 B
AU 200076364	A	20010430	AU 200076364	A	20000929	200142

Priority Applications (No Type Date): US 99156594 A 19990929

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
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WO 200123550	A2	E	60	C12N-015/12	
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Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

AU 200076364	A			C12N-015/12	Based on patent WO 200123550
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Abstract (Basic): WO 200123550 A2

Abstract (Basic):

NOVELTY - An isolated nucleic acid molecule (I) encoding a differentially expressed prostate cancer antigen 3 (PCA3) mRNA containing an additional sequence between exon 3 and exon 4a, giving rise to a long PCA3 mRNA (II), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid molecule (III) consisting of 10-50 nucleotides which specifically hybridize to a differentially expressed (II), and which is, or is complementary to, 10 consecutive nucleotides from the PCA3 nucleotide sequence GAGTAGGAAGGATAGAAACG;

(2) a kit for detecting the presence of differentially expressed PCA3 mRNA in a sample comprising at least one container means having disposed in it, (III);

(3) a recombinant nucleic acid molecule (IV) comprising 5'-3' a promoter effective to initiate transcription in a host cell and (I);

(4) a cell (V) that contains (IV);

(5) a non-human organism that contains (IV);

(6) a purified differentially expressed PCA3 polypeptide (VI), comprising an additional sequence between exon 3 and exon 4a, which interrupts a PCA3 open reading frame, shortening the PCA3 polypeptide, or its epitope-bearing portion;

(7) an antibody (VII) having a specific binding affinity to (VI) or its epitope-bearing portion;

(8) a diagnostic kit comprising a container containing (VII) and a second container containing a conjugate comprising a binding partner of (VII) and a label; and

(9) a hybridoma which produces (VII).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Differentially expressed PCA3 mRNA levels modulator; ex vivo gene therapy; gene therapy.

No biological data is given.

USE - (III) is useful for detecting differentially expressed PCA3 mRNA in a sample which involves contacting the sample with (III) under conditions such that hybridization occurs, and then detecting the presence of the molecule bound to PCA3 mRNA. The quantitation of short

PCA3 mRNA with respect to the long PCA3 mRNA enables a determination of the malignant status of a prostate. (VII) is useful for detecting PCA3 in a sample which involves contacting the sample with (VII) so that immunocomplexes form and detecting the presence of antibody bound to the polypeptide. The differentially expressed PCA3 mRNA is useful for treating prostate cancer in a mammal which involves modulating level of differentially expressed PCA3 mRNA such that the level of (II) is superior to that of a second differentially expressed PCA3 mRNA, which lacks the additional sequence. The differentially expressed PCA3 or RNA or (VI) is useful for diagnosing the presence of predisposition to develop prostate cancer in a patient, which involves, taking a sample from the patient, determining the amount of differentially expressed PCA3 or RNA or PCA3 protein in the sample, and diagnosing the presence or predisposition to develop prostate cancer in a patient. The presence of (II) or the protein is indicative of a non-malignant state of the prostate, and the presence of a short PCA3 mRNA or protein indicate prostate cancer or a predisposition to develop prostate cancer. The differentially expressed PCA3 or RNA or (VI) is also useful for staging prostate cancer in a patient which involves taking a sample from the patient, determining the amount of differentially expressed PCA3 RNA or PCA3 protein in the sample and staging prostate cancer in the patient in which increase in level of short PCA3 mRNA or protein is correlated with an increase in malignancy of prostate cancer. The differentially expressed PCA3 mRNA is useful for assessing the prostate status of a patient which involves quantitatively determining short PCA3 mRNA associated with the malignant state of prostate, and (II) associated with a non-malignant state of prostate, where a level of short PCA3 mRNA with respect to (II) can be correlated to the prostate status of the patient. Preferably, the quantification of the short and long PCA3 mRNA is carried out simultaneously. (All claimed). (VII) is useful for detection and purification purposes and also as a modulator of (VI). (I), (VI) has therapeutic uses. The diagnostic method involving the differentially expressed PCA3 mRNA is useful for a patient suspected of being at risk for developing disease associated with an altered expression level of PCA3 based on family history, or a patient in which it is desired to diagnose a PCA3-related disease. Presymptomatic screening of an individual in need of the screening is made possible by DNA encoding PCA3 protein or PCA3 gene. The screening method allows a presymptomatic diagnosis, of the presence of the PCA3-minus additional sequence, differentially PCA3 mRNA in individuals.

pp; 60 DwgNo 0/4

2/AB/6 (Item 2 from file: 351)  
DIALOG(R) File 351:Derwent WPI  
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012151435

WPI Acc No: 1998-568347/199848

XRAM Acc No: C98-170814

XRPX Acc No: N98-442142

New nucleic acid encoding prostate cancer antigen 3 - for diagnosis, prevention and treatment of prostatic cancer

Patent Assignee: DIAGNOCURE INC (DIAG-N)

Inventor: BUSSEMAKERS M J G

Number of Countries: 083 Number of Patents: 003

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9845420	A1	19981015	WO 98CA346	A	19980409	199848 B
AU 9870194	A	19981030	AU 9870194	A	19980409	199911

EP 1007350	A1	20000614	EP 98916696	A	19980409	200033
			WO 98CA346	A	19980409	

Priority Applications (No Type Date): US 9741836 A 19970410

### Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
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WO 9845420 A1 E 111 C12N-015/00

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU  
CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR  
LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM  
TR TT UA UG US UZ VN YU ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR  
IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9870194      A      C12N-015/00      Based on patent WO 9845420

EP 1007650 A1 E C12N-015/00 Based on patent WO 9845420

Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LI  
LU MC NL PT SE

Abstract (Basic): WO 9845420 A

Isolated nucleic acid (I) encoding prostate cancer antigen 3 (PCA3) is new.

Also new are: (1) nucleic acid (II) of 10-50 nucleotides (nt) that hybridises specifically to RNA or DNA encoding PCA3, comprising, or complementary to, at least 10 consecutive nt of PCA3 exons 1, 2, 3, 4a-4d, provided it does not hybridise to nt 511-985 or 567-961 of a 2037 bp sequence (1) nor to nt 533-1007 or 589-983 of a 3582 bp sequence (6); (2) recombinant nucleic acid (Ia) comprising (I) attached to a promoter or as part of a vector; (3) cells, or non-human organisms, containing (Ia); (4) purified PCA3 polypeptides or their epitope-bearing fragments; (5) antibodies (Ab ) specific for PCA3 or its fragments; (6) hybridomas that produce monoclonal Ab.

USE (II) are used to detect (I) in hybridisation tests, while Ab are used to detect PCA3 in immunoassay tests, for diagnosis, assessment and prognosis of prostatic cancer (PC). Ab, optionally coupled to a cytotoxin or radioisotope, and nucleic acid antisense to (I) can be used to treat PC, while determining elevated levels of PCA3 (as RNA or protein) can be used to detect a predisposition to development of PC, e.g. in prenatal tests. PCA3 and its fragments are useful in vaccines to prevent PC; to raise or detect Ab; in drug screens to identify specific (ant)agonists (potentially useful therapeutically) and for studying protein-DNA interactions. Cells of (3) are used to produce recombinant PCA3 and the transgenic animals are models for human disease.

ADVANTAGE - Detecting PCA3 allows differentiation between malignant and benign prostatic disease, and the level of PCA3 expression is correlated with the grade of tumour.

Dwg. 1/5

2/AB/7 (Item 1 from file: 357)  
DIALOG(R) File 357:Derwent Biotechnology Abs  
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0268640 DBA Accession No.: 2001-08946 PATENT  
Novel nucleic acid encoding differentially expressed prostate cancer  
antigen-3 mRNA containing additional sequence giving rise to long PCA3  
mRNA, useful for diagnosis of mammal afflicted with prostate cancer  
- vector-mediated gene transfer, expression in host cell, monoclonal  
antibody, hybridoma, agonist, antagonist and transgenic animal for drug  
screening and gene therapy  
AUTHOR: Busse U; Chypre C; Fradet Y

CORPORATE SOURCE: Sainte-Foy, Quebec, Canada.

PATENT ASSIGNEE: Diagnocure 2001

PATENT NUMBER: WO 200123550 PATENT DATE: 20010405 WPI ACCESSION NO.:  
2001-258132 (2026)

PRIORITY APPLIC. NO.: US 156594 APPLIC. DATE: 19990929

NATIONAL APPLIC. NO.: WO 2000CA1154 APPLIC. DATE: 20000929

LANGUAGE: English

ABSTRACT: An isolated DNA molecule (I) encoding a differentially expressed prostate cancer antigen-3 (PCA3) mRNA containing an additional sequence between exon-3 and exon-4a, giving rise to a long PCA3 mRNA (II), is claimed. Also claimed are: an isolated DNA molecule (III) consisting of 10-50 specific nucleotides; a kit for detecting the presence of differentially expressed PCA3 mRNA in a sample containing (III); a recombinant DNA (IV) containing, 5'-3', a promoter effective to initiate transcription in a host cell and (I); a cell that contains (IV); a non-human organism that contains (IV); a purified differentially expressed PCA3 protein (VI), containing an additional sequence between exon-3 and exon-4a, which interrupts a PCA3 open reading frame, shortening the PCA3 protein, or its epitope bearing portion; antibody (VII) specific to (VI); a diagnostic kit containing (VII); and a hybridoma which produces (VII). (III) is useful for detecting differentially expressed PCA3 mRNA in a sample and for gene therapy and treating prostate cancer in a mammal. Also disclosed are: a vector; screening assays; agonists and antagonists; fusion proteins; and pharmaceutical compositions. (60pp)

2/AB/8 (Item 2 from file: 357)

DIALOG(R) File 357:Derwent Biotechnology Abs

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0230406 DBA Accession No.: 99-00507 PATENT

New nucleic acid encoding prostate cancer antigen-3- vector-mediated gene transfer and expression in host cell or transgenic animal, monoclonal antibody preparation by hybridoma cell culture and DNA probe

AUTHOR: Bussemakers M J G

CORPORATE SOURCE: Ste-Foy, Quebec, Canada.

PATENT ASSIGNEE: Diagnocure 1998

PATENT NUMBER: WO 9845420 PATENT DATE: 981015 WPI ACCESSION NO.:  
98-568347 (9848)

PRIORITY APPLIC. NO.: US 41836 APPLIC. DATE: 970410

NATIONAL APPLIC. NO.: WO 98US346 APPLIC. DATE: 980409

LANGUAGE: English

ABSTRACT: A new and specified DNA sequence encodes prostate cancer antigen - 3 . Also claimed are: DNA that hybridizes to the new sequence and cDNA; recombinant DNA containing the new sequence attached to a promoter or as part of a vector; cells or non-human organisms containing the DNA; purified proteins or epitope-bearing fragments; antibodies specific for the protein; and hybridomas that produce monoclonal antibodies. The new protein may be used to detect the DNA in hybridization tests, (e.g. using DNA probes), or for diagnosis or prognosis of prostate cancer. The antibodies, optionally coupled to a cytotoxin or radioisotope, and nucleic acid antisense to the new sequence, may be used to treat prostate cancer. The protein may be used in a recombinant vaccine or for drug screening. Transgenic animals containing the DNA may be used as models for human disease, and the DNA may be used for gene therapy. (111pp)

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